#### PATENT COOPERATION TREATY

# ROC'd POWPTO 08 DEC 2004

From the INTERNATIONAL SEARCHING AUTHORITY	PCT
To:  KRIC POTTER CLARKSON Attn. Pilkington, Stephanie Park View House 58 The Ropewalk Nottingham NG1 5DD	OR THE DECLARATION
UNITED KINGDOM PARTNES ACTO	ONED
	Date of mailing (day/month/year) 21/06/2004
Applicant's or agent's file reference	FOR FURTHER ACTION See paragraphs 1 and 4 below
DUNY/P28395PC International application No.	International filing date (day/month/year) 09 / 06 / 2003
PCT/GB 03/02509	(day/month/year) 09/06/2003
Applicant UNIVERSITY OF DUNDEE	
The applicant is hereby notified that the International Search Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claims When? The time limit for filing such amendments is normal	s of the International Application (see Rule 46):
International Search Report; however, for more det	tails, see the notes on the accompanying sheet.
Where? Directly to the International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Fascimile No.: (41-22) 740.14.35	
For more detailed instructions, see the notes on the accordance	•
The applicant is hereby notified that no International Search Article 17(2)(a) to that effect is transmitted herewith.	n Report will be established and that the declaration under
3. With regard to the protest against payment of (an) addition	onal fee(s) under Rule 40.2, the applicant is notified that:
the protest together with the decision thereon has been applicant's request to forward the texts of both the protest.	n transmitted to the International Bureau together with the test and the decision thereon to the designated Offices.
no decision has been made yet on the protest; the app	viicant will be notified as soon as a decision is made.
Further action(s): The applicant is reminded of the following:     Shortly after 18 months from the priority date, the international at	polication will be nublished by the International Bureau.
If the applicant wishes to avoid or postpone publication, a notice priority claim, must reach the International Bureau as provided completion of the technical preparations for international publications.	in Rules 90 <i>bis</i> .1 and 90 <i>bis</i> .3, respectively, before the ation.
Within 19 months from the priority date, a demand for internation wishes to postpone the entry into the national phase until 30 mo	onins from the phonity date (in some Offices even Tales).
Within 20 months from the priority date, the applicant must perforbefore all designated Offices which have not been elected in the priority date or could not be elected because they are not bound	te demand of in a fatel election within 19 months nomine
Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Marilú Masserut

Form PCT/ISA/220 (July 1998)



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These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

in these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

#### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before During the international preaminary Examining Authority. The description and drawings may only be amended under Article 34 before the international Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.



The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

the claim is unchanged;

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- the claim is cancelled; (ii)
- (iii) the claim is new;
- the claim replaces one or more claims as filed; (iv)
- the claim is the result of the division of a claim as filed.

The following examples Illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]: "Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
- [Where originally there were 15 claims and after amendment of all claims there are 11]: Claims 1 to 15 replaced by amended claims 1 to 11."
- [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
- [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

#### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

it must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

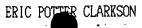
### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement ) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

#### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.



# PATENT COOPERATION TREATY

# **PCT**

#### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference DUNY/P28395PC	FOR FURTHER see Notification of (Form PCT/ISA/2	of Transmittal of International Search Report (20) as well as, where applicable, item 5 below.
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/GB 03/02509	09/06/2003	08/06/2002
Applicant		
·		
UNIVERSITY OF DUNDEE		·
This International Search Report has according to Article 18. A copy is bein	been prepared by this International Searching Aut g transmitted to the International Bureau.	nortty and is transmitted to the applicant
This International Search Report cons	sists of a total of 9 sheets.	
It is also accompanies	d by a copy of each prior art document cited in this	report.
Basis of the report		·
With regard to the language, language in which it was filed.	the international search was carried out on the bas unless otherwise indicated under this item.	is of the international application in the
the international seam Authority (Rule 23.1(t	ch was carried out on the basis of a translation of ti oi)).	he international application furnished to this
b. With regard to any nucleofide was carried out on the basis of	e and/or amino acid sequence disclosed in the in of the sequence listing:	temational application, the international search
contained in the intern	national application in written form.	
	international application in computer readable for	n.
1	tly to this Authority in written form.	
X furnished subsequent	by to this Authority in computer readble form.	
X the statement that the international application	e subsequently furnished written sequence listing don as filed has been furnished.	oes not go beyond the disclosure in the
		s identical to the written sequence listing has been
/ L	tound unsearchable (See Box I).	
3. X Unity of invention is	lacking (see Box II).	
4. With regard to the title,	•	
· • • • • • • • • • • • • • • • • • • •	s submitted by the applicant.	
X the text has been est	ablished by this Authority to read as follows:	
METHOD FOR DESIGNI	NG PDK1 MODULATORS	
		<u> </u>
5. With regard to the abstract,		
	s submitted by the applicant.	
the text has been est	ablished, according to Rule 38.2(b), by this Authori n the date of mailing of this international search rep	ty as it appears in Box III. The applicant may, port, submit comments to this Authority.
• .	published with the abstract is Figure No.	
as suggested by the		X None of the figures.
1 —	n failed to suggest a figure.	
1 . L.	etter characterizes the invention.	
Decause this figure of	THE CHARACTERS INC BIACTERIE	

Form PCT/ISA/210 (first sheet) (July 1998)



International application No. PCT/GB 03/02509

TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

A mehod for selecting or designing a compound for modulating the activity of phosphoinositide dependent protein kinase 1 (PDK1), the method comprising the step of using molecular modelling means to select of design a compound that is predicted to interact with the protein kinase catalytic domain of PDK1, wherein a three-dimensional structure or at least a part of the protein kinase catalytic domain of PDK1 is compared with a three-dimensional structure of a compound, and a compound that is predicted to interact with the said protein kinase catalytic domain is selected, wherein the threedimensional structure of at least a part of the protein kinase catalytic domain of PDK1 is a three-dimensional structure (or part thereof) determined for a polypeptide consisting of residues equivalent to residues 51 to 359 of full lenght human PKD1, or fragment or fusion thereof.

International application No. PCT/GB 03/02509

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Into	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: 17,18,37 because they relate to subject matter not required to be searched by this Authority, namely:
	Claim 17 and 18: Rule 39.1(i) PCT - Mathematical method Claim 37: Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
	39.1(1V) PCI - Mechod for creatment of the human of annual body by therapy
2. X	Claims Nos.:  because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
	see FURTHER INFORMATION sheet PCT/ISA/210
з. 🗌	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
•	
Box II	Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)
This Inte	emational Searching Authority found multiple inventions in this international application, as follows:
1125	
	see additional sheet
:	
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. 🗌	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
•	
<i>:</i> .	
-	
4: X	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
	1-16, 38-42(fully); 33-37 (partially)
Remark	con Protest The additional search fees were accompanied by the applicant's protest.
* -	No protest accompanied the payment of additional search fees.

International Application No. PCT/ GB 03/02509

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-16, 38-42 (fully); 33-37 (partially)

A method of selecting compounds modulating the activity of PDK1-like kinases, the compounds identified with the method and the use of these compounds.

2. Claims: 17-18 (fully)

A method to assess the activation state of a protein kinase, based on the structure coordinates.

3. Claims: 19-32 (fully); 33-37 (partially)

Mutated PDK1-like protein kinases, wherein specific residues of the hydrofobic pocket or phosphate binding pocket are mutated.

International Application No. PCT/ GB 03/02509

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 33, 34 (in full); 35-37 (in part, in as far as referring back to claim 33)

Present claims 33, 34 (in full) and claims 35-37 (in part, in as far as referring back to claim 33) relate to a compound defined by reference to a desirable characteristic or property, namely "identified or identifiable by a method according to claims 1-16, 28 or 29"

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for no such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the screening methods per se.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

International Application No PCT/GB 03/02509

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12Q1/48 G06F19/00 C07K14/00

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C12N9/12

C12N5/00

C07K16/00

According to International Patent Classification (IPC) or to both national classification and IPC

Minimum documentation searched (classification system followed by classification symbols)

C12Q C07K C12N G06F **1PC 7** 

Occurrentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE

C. De	CUMENTS CONSIDERED TO BE RELEVANT	
Cate	ory * Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
) <b>A</b>	WO 01/44497 A (UNIV DUNDEE ;ALESSI DARIO (GB); BIONDI RICARDO (GB)) 21 June 2001 (2001-06-21) cited in the application abstract; claims 1-63 figure 15	1-16, 35-42
	page 5, line 19 - line 30 page 7, line 16 - line 30; table 1 page 13, line 26 -page 14, line 7 page 16, line 25 -page 18, line 30 page 19, line 20 -page 20, line 2 page 27, line 13 - line 30 page 29, line 11 -page 30, line 10	
	page 31, line 1 - line 6 page 32, line 10 - line 17 page 36, line 9 -page 37, line 2 page 39, line 16 - line 23 page 41, line 16 -page 42, line 5 page 43, line 8 - line 30	

Further documents are listed in the continuation of box C. X

Patent family members are listed in annex.

Special categories of cited documents:

- "A" document defiring the general state of the art which is not considered to be of particular relevance
- earlier document but published on or after the international
- document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- document published prior to the international filing date but later than the priority date claimed
- T later document published after the international filling date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

25 February 2004

Date of mailing of the international search report

Authorized officer

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Riswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

Vanhalst, K

Form PCT/ISA/210 (second sheet) (January 2004)

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International Application No PCT/GB 03/02509

Content   College   Coll			-1/GB 03/02509
A WO 01/35316 A (RAMNARAYAN KALYANARAMAN ;STRUCTURAL BIOINFORMATICS INC (US); HESS) 17 May 2001 (2001-05-17) abstract; Claims 1-63 page 3, line 10 -page 9, line 19 page 36, line 10 - line 15 page 40, line 23 -page 41, line 25 page 56, line 25 -page 53, line 2  A WO 01/71347 A (GODDARD WILLIAM A			Relevant to claim No.
A WO 01/35316 A (RAMNARAYAN KALYANARAMAN ;STRUCTURAL BIOINFORMATICS INC (US); HESS) 17 May 2001 (2001-05-17) abstract; claims 1-63 page 3, line 10 - page 9, line 19 page 36, line 10 - line 15 page 40, line 23 -page 41, line 25 page 56, line 25 -page 53, line 2  A WO 01/71347 A (GODDARD WILLIAM A III; WAIDEHI NAGARAJAN; FLORIANO WELY B; CALIFORNIA I) 27 September 2001 (2001-09-27) abstract; claims 1-35 examples 1-5 page 3, line 24 -page 12, line 14  A US 5 854 992 A (DEWITTE ROBERT S ET AL) 29 December 1998 (1998-12-29) abstract column 1, line 5 - line 13 column 2, line 23 - line 36 column 3, line 38 -column 18, line 8 claims 1-10,12-18  A WO 02/22793 A (ABELL CHRISTOPHER; BLUNDELL TOM L (GB); ASTEX TECHNOLOGY LTD (GB);) 21 March 2002 (2002-03-21) abstract; claims 1-11 page 1, line 5 - line 17 page 3, line 12 -page 4, line 25 page 5, line 9 -page 7, line 22 page 8, line 5 - line 12 page 9, line 9-page 7, line 22 page 12, line 1 - line 20 page 12, line 13 - line 13 page 15, line 1 - line 35 page 21, line 13 -page 33, line 26  A WO 98/41638 A (MEDICAL RES COUNCIL) 24 September 1998 (1998-02-44) cited in the application abstract; claims 1-36 page 2, line 11 - line 14 page 25, line 15 - line 28 page 25, line 16 - line 28 page 27, line 20 -page 25		45 line 10 mags 50 line 10	
STRUCTURAL BIOINFORMATICS INC (US); HESS)   17 May 2001 (2001-05-17)   abstract; claims 1-63   page 3, line 10 - page 9, line 19   page 36, line 10 - page 11 ine 15   page 40, line 23 - page 41, line 25   page 50, line 25 - page 53, line 2	A		1-16,
page 3, line 10 -page 9, line 19 page 36, line 16 - line 15 page 40, line 23 -page 41, line 25 page 50, line 25 -page 53, line 2  A		;STRUCTURAL BIOINFORMATICS INC (US); HESS) 17 May 2001 (2001-05-17)	35-42
page 50, line 25 -page 53, line 2  MO 01/71347 A (GODDARD WILLIAM A III; VAIDENI NAGARAJAN; FLORIANO WELY B; CALIFORNIA I) 27 September 2001 (2001-09-27) abstract; claims 1-35 examples 1-5 page 3, line 24 -page 12, line 14  A US 5 854 992 A (DEWITTE ROBERT S ET AL) 29 December 1998 (1998-12-29) abstract column 1, line 5 - line 13 column 2, line 23 -column 5, line 31 column 8, line 29 -column 18, line 8 claims 1-10,12-18  A W0 02/22793 A (ABELL CHRISTOPHER; BLUNDELL TOM L (GB); ASTEX TECHNOLOGY LTD (GB); 21 March 2002 (2002-03-21) abstract; claims 1-11 page 1, line 5 - line 12 page 3, line 12 -page 4, line 25 page 5, line 9 -page 7, line 22 page 8, line 5 - line 12 page 9, line 25 -page 10, line 9 page 11, line 10 - line 20 page 11, line 11 -page 33, line 26  A W0 98/41638 A (MEDICAL RES COUNCIL) 24 September 1998 (1998-09-24) cited in the application abstract; claims 1-36 page 25, line 15 - line 14 page 21, line 26 -page 22, line 15 page 25, line 15 - line 28 page 27, line 26 -page 25		page 3, line 10 -page 9, line 19	
III; VAIDEHI MAGARAJAN; FLORIANO WELY B; CALIFORNIA I) 27 September 2001 (2001-09-27) abstract; claims 1-35 examples 1-5 page 3, line 24 -page 12, line 14  A US 5 854 992 A (DEWITTE ROBERT S ET AL) 29 December 1998 (1998-12-29) abstract column 1, line 5 - line 13 column 2, line 23 - line 36 column 3, line 38 -column 5, line 31 column 8, line 29 -column 18, line 8 claims 1-10;12-18  A WO 02/22793 A (ABELL CHRISTOPHER ;BLUNDELL TOM L (GB); ASTEX TECHNOLOGY LTD (GB);) 21 March 2002 (2002-03-21) abstract; claims 1-11 page 1, line 5 - line 7 page 3, line 12 -page 4, line 25 page 9, line 9-page 7, line 22 page 8, line 5 - line 12 page 9, line 25 -page 10, line 9 page 11, line 10 - line 20 page 12, line 3 - line 13 page 15, line 1 - line 35 page 21, line 13 -page 33, line 26  A WO 98/41638 A (MEDICAL RES COUNCIL) 24 September 1998 (1998-09-24) cited in the application abstract; claims 1-36 page 2, line 15 - line 28 page 25, line 15 - line 28 page 27, line 26 -page 22, line 15 page 27, line 20 -page 25		page 40, line 23 -page 41, line 25 page 50, line 25 -page 53, line 2	
27 September 2801 (2801-09-27) abstract; claims 1-35 examples 1-5 page 3, line 24 -page 12, line 14  A US 5 854 992 A (DEWITTE ROBERT S ET AL) 29 December 1998 (1998-12-29) abstract column 1, line 5 - line 13 column 2, line 23 - line 36 column 2, line 38 -column 5, line 31 column 8, line 29 -column 18, line 8 claims 1-10,12-18  A WO 02/22793 A (ABELL CHRISTOPHER; BLUNDELL TOM L (6B); ASTEX TECHNOLOGY LTD (GB);) 21 March 2002 (2002-03-21) abstract; claims 1-11 page 1, line 5 - line 7 page 3, line 12 -page 4, line 25 page 5, line 9 -page 7, line 22 page 8, line 5 - line 12 page 9, line 25 -page 10, line 9 page 11, line 10 - line 20 page 12, line 3 - line 13 page 15, line 1 - line 23 page 21, line 13 -page 33, line 26  A WO 98/41638 A (MEDICAL RES COUNCIL) 24 September 1998 (1998-09-24) cited in the application abstract; claims 1-36 page 2, line 11 - line 14 page 21, line 26 -page 22, line 15 page 27, line 28	A	III; VAIDEHI NAGARAJAN; FLORIANO WELY B;	
page 3, line 24 -page 12, line 14  US 5 854 992 A (DEWITTE ROBERT S ET AL) 29 December 1998 (1998-12-29) abstract column 1, line 5 - line 13 column 2, line 23 - line 36 column 3, line 38 -column 5, line 31 column 8, line 29 -column 18, line 8 claims 1-10,12-18  A WO 02/22793 A (ABELL CHRISTOPHER; BLUNDELL TOM L (GB); ASTEX TECHNOLOGY LTD (GB);) 21 March 2002 (2002-03-21) abstract; claims 1-11 page 1, line 5 - line 7 page 3, line 12 -page 4, line 25 page 5, line 9 -page 7, line 22 page 8, line 5 - line 12 page 9, line 25 -page 10, line 9 page 11, line 10 - line 20 page 12, line 3 - line 13 page 15, line 1 - line 35 page 21, line 13 -page 33, line 26  A WO 98/41638 A (MEDICAL RES COUNCIL) 24 September 1998 (1998-09-24) cited in the application abstract; claims 1-36 page 2, line 11 - line 14 page 21, line 26 -page 22, line 15 page 27, line 20 -page 25		27 September 2001 (2001-09-27) abstract; claims 1-35	
29 December 1998 (1998-12-29) abstract column 1, line 5 - line 13 column 2, line 23 - line 36 column 3, line 38 -column 5, line 31 column 8, line 29 -column 18, line 8 claims 1-10,12-18  A WO 02/22793 A (ABELL CHRISTOPHER ;BLUNDELL TOM L (GB); ASTEX TECHNOLOGY LTD (GB);) 35-42 21 March 2002 (2002-03-21) abstract; claims 1-11 page 1, line 5 - line 7 page 3, line 12 -page 4, line 25 page 5, line 9 -page 7, line 22 page 8, line 5 - line 12 page 9, line 25 -page 10, line 9 page 11, line 10 - line 20 page 12, line 3 - line 13 page 15, line 1 - line 35 page 21, line 13 -page 33, line 26  A WO 98/41638 A (MEDICAL RES COUNCIL) 24 September 1998 (1998-09-24) cited in the application abstract; claims 1-36 page 2, line 11 - line 14 page 21, line 26 -page 22, line 15 page 25, line 15 - line 28 page 27, line 20 -page 25		page 3, line 24 -page 12, line 14	
Column 1, line 5 - line 13	A	29 December 1998 (1998-12-29) abstract	
Column 8, line 29 -column 18, line 8   Claims 1-10,12-18		column 1, line 5 - line 13 column 2, line 23 - line 36	
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